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MINIREVIEWS

Regional dynamic cerebral autoregulation across anterior and posterior circulatory territories: A detailed exploration and its clinical implications

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Abstract

Cerebral autoregulation (CA) is the mechanism that maintains stable cerebral blood flow (CBF) despite fluctuations in systemic blood pressure, crucial for brain homeostasis. Recent evidence highlights distinct regional variations in CA between the anterior (carotid) and posterior (vertebrobasilar) circulations. Non-invasive neuromonitoring techniques, such as transcranial Doppler, transfer function analysis, and near-infrared spectroscopy, facilitate the dynamic assessment of CBF and autoregulation. Studies indicate a robust autoregulatory capacity in the anterior circulation, characterized by rapid adjustments in vascular resistance. On the contrary, the posterior circulation, mainly supplied by the vertebral arteries, may have a lower autoregulatory capacity. in acute brain injuries such as intracerebral and subarachnoid hemorrhage, and traumatic brain injuries, dynamic CA can be significantly altered in the posterior circulation. Proposed physiological mechanisms of impaired CA in the posterior circulation include: (1) Decreased sympathetic innervation of the vasculature impairing compensatory vasoreactivity; (2) Endothelial dysfunction; (3) Increased cerebral metabolic rate of oxygen consumption within the visual cortex causing CBF-metabolism (*i.e.*, neurovascular) uncoupling; and (4) Impaired blood-brain barrier integrity leading to impaired astrocytic mediated release of vasoactive substances (*e.g.* nitric oxide, potassium, and calcium ions). Furthermore, more research is needed on the effects of collateral circulation, as well as the circle of Willis variants, such as the fetal-type posterior cerebral artery, on dynamic CA. Improving our understanding of these mechanisms is crucial to improving the diagnosis, prognosis, and management of various cerebrovascular disorders.

Key Words: Cerebral autoregulation; Anterior circulation; Posterior circulation; Posterior

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cerebral artery; Regional cerebral autoregulation; Transcranial doppler; Near-infrared spectroscopy; Transfer function analysis; Cerebral energetics

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Core Tip: Cerebral autoregulation (CA) maintains stable cerebral blood flow (CBF) despite systemic blood pressure changes. Recent evidence highlights regional CA variations between anterior and posterior circulations. Non-invasive neuromonitoring techniques like transcranial Doppler, transfer function analysis, and near-infrared spectroscopy facilitate dynamic CBF assessment. Studies show robust autoregulation in the anterior circulation but lower capacity in the posterior circulation. Impaired CA in the posterior circulation, especially during acute brain injuries, may result from decreased sympathetic innervation, endothelial dysfunction, increased metabolic demands, and impaired blood-brain barrier integrity. Understanding these mechanisms is vital for improving cerebrovascular disorder management.

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INTRODUCTION

Cerebral autoregulation (CA), the inherent property of the cerebral vasculature to maintain relatively constant cerebral blood flow (CBF) following fluctuations in cerebral perfusion pressure (CPP), and is crucial to maintaining normal brain function[1]. This dynamic process ensures that the brain receives an adequate blood supply to meet its metabolic demands while preventing hyperperfusion or hypoperfusion-induced damage[2]. However, emerging evidence suggests that CA may vary in different circulatory territories within the brain, with implications for neurological function and clinical outcomes.

Recent studies have indicated differential cerebral autoregulatory mechanisms between the anterior and posterior circulatory territories of the brain[3]. The anterior circulation, supplied primarily by the internal carotid arteries and their branches, encompasses critical regions such as the frontal, parietal, and temporal lobes, as well as deep structures including the basal ganglia and internal capsule. On the contrary, the posterior circulation, which is primarily served by the vertebral and basilar arteries, supplies vital structures such as the brainstem, cerebellum, and posterior cerebral hemispheres[2]. Understanding the nuanced differences in autoregulatory behavior between these different circulatory territories is essential to elucidate the pathophysiology of various neurological conditions and guide clinical management strategies[4]. Furthermore, such knowledge may have profound implications for the development of targeted therapeutic interventions aimed at optimizing cerebral perfusion and mitigating the risk of ischemic or hemorrhagic brain injury[5]. Studying CA clinically is crucial because it directly impacts the management of patients with neurological conditions such as stroke, traumatic brain injury (TBI), and subarachnoid hemorrhage. Variations in autoregulatory function between different regions of the brain can influence clinical outcomes, particularly in conditions affecting the posterior circulation, where critical structures like the brainstem and cerebellum are highly vulnerable to dysregulated blood flow.

In this manuscript, we undertake a detailed exploration of regional CA across anterior and posterior circulatory territories. Drawing on a comprehensive review of existing literature, we seek to identify the underlying physiological principles governing regional variations in autoregulatory function and their clinical relevance. By synthesizing current evidence and identifying key research gaps, our objective is to provide valuable information on the intricate interplay between cerebral hemodynamics, energetics, and circulatory anatomy.

OVERVIEW OF CA

Lassen's curve, proposed by the Danish physiologist Niels A. Lassen, is a graphical representation of the relationship between CBF and CPP. It represents the autoregulatory capacity of the cerebral vasculature over a range of CPP values. In the classic representation, Lassen's curve shows a sigmoidal shape, indicating that CBF remains relatively constant within a certain range of CPP, but begins to decrease at lower CPP values and plateau at higher CPP values[6] (Figure 1).

Although Lassen's curve has been instrumental in understanding CA, it is not without its criticisms. The autoregulatory curve assumes a linear relationship between CPP and CBF within the autoregulatory range[7]. However, autoregulatory mechanisms often exhibit non-linear behavior, especially under extreme physiological conditions or in the presence of cerebrovascular disease. Lassen's curve does not account for the temporal dynamics of CA, including the time constants associated with vascular responses to changes in CPP. Dynamic models, such as transfer function analysis, provide a more complete understanding of autoregulatory dynamics over a range of frequencies[5]. Despite these criticisms, Lassen's curve remains a valuable conceptual tool for illustrating the principles of CA. However, its limitations

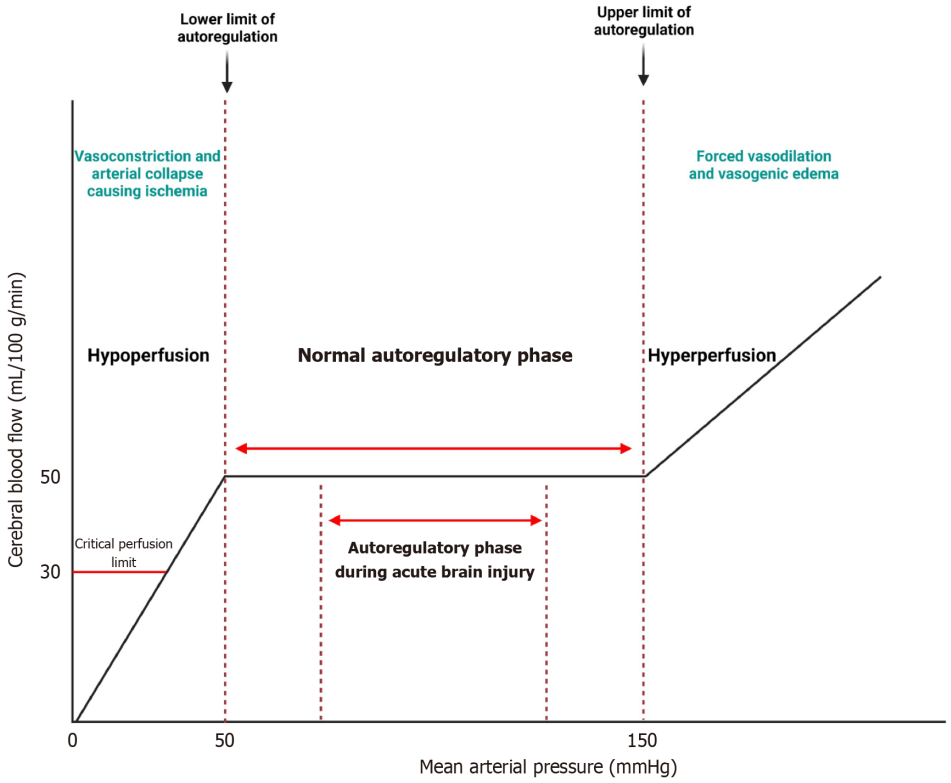

Figure 1 Lassen's cerebral autoregulatory curve. Cerebral blood flow is normally reported to remain constant over a large mean arterial pressure range of 50-150 mmHg. This range is significantly shifted or narrower in patients with acute brain injury. The ischemic critical perfusion threshold is defined at 30 mL/100 g/min. This figure was generated using BioRender (Agreement No: SE269MFWGB).

underscore the need for more sophisticated modeling approaches and dynamic assessments of autoregulatory function in clinical practice.

MECHANISMS OF CA

CA is maintained through the intricate interplay of several physiological mechanisms, including myogenic, metabolic, and neurogenic factors.

Myogenic mechanism

The myogenic mechanism is based on the inherent contractility of cerebral arterioles in response to changes in intravascular pressure. When systemic blood pressure (BP) increases, arteriolar smooth muscle contracts, reducing vessel diameter and limiting blood flow to the cerebral microcirculation. In contrast, a decrease in systemic BP causes vasodilation, allowing increased CBF to maintain adequate perfusion[8].

Metabolic mechanism

Metabolic factors, such as changes in tissue O_2 tension, CO_2 levels, and pH, also influence CA. Increased metabolic activity, as seen during neuronal activation, leads to local vasodilation to meet the increased demand for oxygen and nutrients. In contrast, the accumulation of metabolic by-products, such as CO_2, triggers vasodilation to improve cerebral perfusion and facilitate waste removal[9].

Neurogenic mechanism

Neurogenic factors, including sympathetic and parasympathetic innervation, play a role in modulating cerebral vascular tone. Sympathetic stimulation typically induces vasoconstriction, while parasympathetic activity promotes vasodilation. These autonomic influences help regulate CBF in response to physiological and environmental stimuli[10].

CLINICAL RELEVANCE OF CA

Understanding the principles of CA is essential for the management of various neurological conditions, including TBI, stroke, and neurodegenerative diseases. Impairments in autoregulatory function can predispose individuals to cerebral

ischemia or edema, exacerbating neurological injury. Throughout the years a patient oriented CPP-protocol 'CPP_{OPT}' has been proposed to optimize individual CA across various acute brain injuries. Steiner *et al*[11] was the first to introduce the term CPP_{OPT} in 2002[11]. CPP_{OPT} represents the ideal range of CPP in which autoregulation is most effective in maintaining stable CBF while minimizing the risk of hypoperfusion or cerebral hyperperfusion. Determining CPP_{OPT} involves dynamic monitoring of cerebral autoregulatory function using techniques such as transcranial Doppler ultrasound (TCD) or near-infrared spectroscopy (NIRS) to assess the relationship between CPP and CBF. By identifying the CPP range associated with the most favorable autoregulatory response, clinicians can tailor BP management strategies to maintain the CPP within this optimal range, thus reducing the risk of secondary brain injury. CPP_{OPT}-guided hemodynamic management has shown promise in improving outcomes in patients with TBI, subarachnoid hemorrhage, and ischemic stroke by preventing cerebral hypoperfusion and minimizing the occurrence of secondary insults.

The pressure reactivity index (PRx) is a valuable metric in neurocritical care that provides information on the dynamic relationship between intracranial pressure (ICP) and CPP. Lang *et al*[12] introduced the PRx to assess CA and is often used in neurocritical care scenarios[12]. PRx is calculated as the moving correlation coefficient between slow waves of ICP and CPP and reflects the ability of the cerebrovascular system to autoregulate in response to changes in BP. In neurocritical care, PRx serves as a surrogate marker for CA, allowing clinicians to assess the brain's ability to maintain stable CBF during a range of BP fluctuations. A positive PRx value indicates impaired autoregulation, since increases in ICP are associated with decreases in CPP, suggesting a passive response of the cerebral vasculature to changes in perfusion pressure[13]. On the contrary, a negative PRx value suggests intact autoregulation, with increases in ICP accompanied by compensatory increases in CPP to maintain stable CBF[14].

In Petersen *et al*'s study[15], the authors investigated the efficacy of personalized autoregulation-based BP targets compared to static systolic BP thresholds in patients undergoing endovascular thrombectomy for acute ischemic stroke. Using tissue oxygenation derived from NIRS to measure autoregulatory function, personalized limits of autoregulation were successfully computed for the 90 patients. The study found that the percentage of time with mean arterial pressure (MAP) exceeding the upper limit of autoregulation was significantly associated with worse 90-day outcomes, particularly in patients with hemorrhagic transformation. Although there was a trend toward worse outcomes with increasing time above fixed systolic BP thresholds, the effect sizes were smaller compared to the personalized approach. The study concludes that deviation from the BP targets based on personalized autoregulation can increase the risk of further brain injury and poor functional outcomes, suggesting that this approach may present a better strategy for hemodynamic management in patients with acute ischemic stroke compared to the classical approach of maintaining systolic BP below a predetermined value[15].

Svedung Wettervik *et al*[16] conducted an observational study aiming to investigate the combined effect of insult intensity and duration, specifically focusing on ICP, PRx, CPP, and CPP_{opt} on clinical outcomes in pediatric TBI. The study included 61 pediatric patients with severe TBI between 2007 and 2018, with at least 12 hours of ICP data in the first 10 days after injury. The results indicated that brief episodes of ICP > 25 mmHg and longer episodes (20 minutes) of ICP between 20-25 mmHg were associated with unfavorable results. Similarly, higher PRx values, especially for longer durations, were correlated with worse outcomes. A transition was observed from favorable to unfavorable outcomes for CPP < 50 mmHg, with no association found for high CPP values. Furthermore, deviations from CPP_{opt} below -10 mmHg were associated with worse outcomes, suggesting a potential role for autoregulatory-oriented management in pediatric TBI[16].

MATHEMATICAL ASSESSMENT OF CA

Various mathematical approaches have been employed to characterize CA, including linear and non-linear models, which aim to capture the complex interactions between physiological parameters governing cerebrovascular dynamics. Linear transfer function analysis is a commonly used method to assess CA by analyzing the frequency-dependent relationship between CPP and CBF fluctuations. The transfer function *H(f)* represents the transfer of pressure fluctuations to CBF fluctuations at different frequencies, typically in the range of 0.03-0.15 Hz, corresponding to the low-frequency range of autoregulatory responses[17].

The transfer function is defined as: $H(f) = P(f)/CBF(f)$, where $P(f)$ and $CBF(f)$ represent the fourier transformations of the CPP and CBF signals, respectively. Gain and phase change of the transfer function provide information on the magnitude and timing of CBF responses to changes in CPP.

Nonlinear models offer a more comprehensive representation of dynamic CA by capturing the nonlinearities inherent in cerebrovascular regulation. One such approach is the autoregulatory index (ARI), which quantifies the relationship between CPP and CBF over a range of pressures.

The ARI is calculated as: ARI = CBF/CPP.

ARI values close to zero indicate intact autoregulation, while deviations from zero suggest impaired autoregulatory function.

The relationship between CBF, CPP, and cerebrovascular resistance (CVR) can be described by the following equations: CBF = CPP/CVR; CVR = (MAP-ICP)/CBF.

These equations highlight the dependence of CBF on CPP and CVR, emphasizing the importance of maintaining adequate perfusion pressure to ensure sufficient blood flow to the brain.

ANATOMICAL OVERVIEW OF THE POSTERIOR CIRCULATION

The posterior circulation of the brain is primarily supplied by the vertebral arteries, which ascend through the cervical vertebrae and join to form the basilar artery at the base of the brainstem. This system feeds vital structures such as the occipital lobes, cerebellum, brainstem, and part of the thalamus. The vertebral arteries give branches such as the posterior inferior cerebellar artery, while the basilar artery gives rise to branches including the anterior inferior cerebellar arteries, pontine arteries, and superior cerebellar arteries, culminating in the posterior cerebral arteries that supply the posterior cerebral hemispheres. Pathologies in this circulation, such as brain stem strokes or cerebellar infarctions, significantly impact motor control and vital functions, underscoring the clinical importance of understanding the unique autoregulatory dynamics of these territories[18,19].

COLLATERAL VESSELS AND CIRCLE OF WILLIS VARIANTS AND DYNAMIC CA

The cerebral collateral circulation, particularly the anterior communicating artery (ACoA) and the posterior communicating artery (PCoA), plays a crucial role in maintaining CBF and autoregulation, especially in the context of arterial stenosis or occlusion. These collateral vessels provide alternative pathways for blood flow, helping to compensate for impaired perfusion and preserve neurological function.

The ACoA connects the left and right anterior cerebral arteries, forming a vital component of the Circle of Willis. It allows crossflow between the hemispheres, which is particularly important in cases of unilateral stenosis or occlusion of the internal carotid artery (ICA). Studies have shown that the presence of patent ACoA significantly enhances the compensatory capacity of the cerebral circulation, maintaining adequate blood flow to the affected hemisphere. In a study by Hartkamp *et al*[20], patients with functional ACoA demonstrated better cerebral hemodynamics and less severe symptoms during carotid artery occlusion compared to those without functional ACoA. The PCoA connects the posterior cerebral artery (PCA) with the internal carotid artery, facilitating collateral flow between the anterior and posterior circulations. Its role becomes critical in conditions such as basilar artery or bilateral vertebral artery stenosis. Research indicates that a patent PCoA can significantly improve dynamic CA by providing an alternative route of blood flow to the posterior circulation[20]. A study by Schomer *et al*[21] demonstrated that people with a well-developed PCoA exhibited better outcomes in terms of maintaining cerebral perfusion in the presence of vertebrobasilar insufficiency[21].

Guo *et al*[22] investigated the influence of ACoA and PCoA on dCA in patients with different types of stenosis. The researchers evaluated dCA using transfer function analysis in 51 patients with ischemic stroke with specific collateral anatomies, divided into two groups based on results of digital subtraction angiography: Group 1 with severe stenosis/occlusion in the basal and/or bilateral vertebral arteries (subdivided by the presence of bilateral PCoAs) and Group 2 with severe stenosis/occlusion in the unilateral internal carotid artery (subdivided by the presence of ACoA and/or PCoAs). The results showed that patients in Group 1 with patent PCoA had significantly higher values of PCA phase difference, indicating better autoregulation, while in Group 2, those with patent ACoA had higher MCA phase difference values. This suggests that the presence of ACoA and PCoA contributes significantly to compensating for impaired dCA, highlighting their crucial role in maintaining stable CBF under stenotic conditions[22].

Srichawla *et al*[23] reported the case of hemorrhagic posterior reversible encephalopathy syndrome (PRES) secondary to chemotherapy. The hemorrhage was present contralateral to a fetal-type PCA (fPCA)[23]. A fPCA has been implicated as an increased risk of stroke and ischemic events[24,25]. Emmert *et al*[26] examined cerebrovascular reserve in 385 healthy participants. Cerebrovascular reserve was decreased ipsilaterally to the fPCA[26]. Taking these results into account, the presence of a fPCA can influence local CA and can play a role in diseases such as PRES and reversible cerebral vasoconstriction syndrome, which have been traditionally understood as loss of CA within the posterior circulation.

SYMPATHETIC INNERVATION OF THE ANTERIOR AND POSTERIOR CIRCULATION

The anterior circulation, which includes the internal carotid arteries and their branches, receives its sympathetic innervation primarily from the superior cervical ganglion. Nerve fibers follow the carotid artery into the skull, forming a network around the vessel known as the carotid plexus. These sympathetic nerves modulate vascular tone by controlling vascular smooth muscle contraction, thus influencing the diameter of the arteries and blood flow to the anterior brain regions such as the frontal, parietal and temporal lobes[27]. On the contrary, the posterior circulation, supplied by the vertebral and basilar arteries, receives sympathetic innervation that is less studied, but believed to be similarly sourced from the superior cervical ganglion, with nerve fibers accompanying the arteries through the foramina in the cervical vertebrae and forming the vertebral plexus. These fibers provide autonomic control over blood flow to critical areas such as the cerebellum, brainstem, and occipital lobes[28].

Differences in sympathetic innervation between the anterior and posterior circulations suggest that autoregulatory mechanisms could also differ between these territories. For example, the anterior regions of the brain, richly innervated, may exhibit a more robust autonomic response to changes in BP, potentially leading to more pronounced vasoconstriction or vasodilation in response to fluctuations in systemic BP. This is supported by studies like those of Hardebo and Owman[29], who demonstrated that the density of sympathetic innervation is higher in the anterior circulation, particularly around the circle of Willis[29]. On the contrary, the posterior circulation might have a different threshold or sensitivity to sympathetic stimulation, which can be crucial in clinical scenarios. For example, the posterior brain regions

are critical for maintaining basic life functions controlled by the brainstem and cerebellum. Dysregulation of sympathetic control in these regions could lead to significant clinical manifestations, such as vertebrobasilar insufficiency or stroke of the posterior circulation, especially under stress or significant hemodynamic changes[30].

PARASYMPATHETIC INNERVATION OF THE ANTERIOR AND POSTERIOR CIRCULATION

The parasympathetic nervous system, primarily through the vagus nerve, plays a significant role in modulating CBF, particularly under resting conditions. Unlike broadly distributed sympathetic innervation, parasympathetic effects on the cerebral circulation are more nuanced and less understood, especially regarding differences between the anterior and posterior circulatory territories. The anterior circulation receives some degree of parasympathetic innervation from the sphenopalatine and otic ganglia. These ganglia release neurotransmitters such as acetylcholine and vasoactive intestinal peptides, which can induce vasodilation of the cerebral arteries. The effect of parasympathetic activation in the anterior circulation is generally considered to promote blood flow during conditions of increased neuronal activity, facilitating neurovascular coupling (NVC) and metabolic regulation[31].

Unlike the anterior circulation, the parasympathetic innervation of the posterior circulation is less understood. It is proposed to be mediated indirectly through local reflex arcs within the brainstem, sensitive to changes in BP and chemical stimuli (*e.g.*, nucleus of the tractus solitarii). This innervation is vital to maintain autonomic functions controlled by the brainstem and cerebellum, affecting the overall hemodynamic stability of these regions[32,33]. Understanding the distinct parasympathetic pathways and their functional implications is crucial to developing targeted therapeutic strategies that address specific cerebral territories, particularly in managing conditions such as vertebrobasilar insufficiency and posterior circulation ischemic events.

NVC AND DYNAMIC CA

NVC refers to the dynamic relationship between neuronal activity and subsequent changes in CBF. This intricate process ensures that the active regions of the brain receive adequate oxygen and nutrients to meet their metabolic demands. NVC may have a close relationship with CA.

NVC involves multiple cell types, including neurons, astrocytes, and vascular endothelial cells, which work together to regulate blood flow. When neurons are activated, they release neurotransmitters that increase the activity of adjacent astrocytes. Astrocytes then release vasoactive substances such as NO, arachidonic acid metabolites and potassium ions, which act on nearby blood vessels to induce vasodilation and increase local blood flow[34]. This response is crucial for rapidly delivering glucose and oxygen to active brain regions. The NVC process can be divided into three primary phases: Initiation, propagation, and resolution. During the initiation of the therapy, neuronal activity leads to the release of signaling molecules that trigger a cascade of events involving astrocytes and endothelial cells. Propagation involves the spread of these signals through the vascular network, resulting in coordinated vasodilation and increased blood flow. Resolution occurs when signaling molecules are cleared and blood vessels return to their baseline state[35].

Impaired NVC is associated with various neurological disorders, including stroke, TBI, and neurodegenerative diseases. For example, in stroke patients, disruptions in NVC can lead to inadequate blood supply to affected brain regions, exacerbating tissue damage and affecting recovery[36]. Similarly, in conditions such as Alzheimer's disease, reduced NVC may contribute to cognitive decline by altering the delivery of nutrients to metabolically active neurons [37]. Recent studies have highlighted the importance of preserving NVC in the management of cerebrovascular disorders. Therapeutic strategies aimed at improving NVC, such as pharmacological agents that promote vasodilation or interventions that support endothelial function, have shown promise in improving outcomes in patients with impaired CA[38]. Additionally, non-invasive imaging techniques, such as functional magnetic resonance imaging and NIRS, are valuable tools for assessing NVC and guiding treatment decisions in clinical settings[39] (Figure 2).

REGIONAL DIFFERENCES IN CEREBRAL ENERGETICS

Cerebral energetics, the study of energy consumption and metabolism in the brain, reveals significant regional differences between the anterior and posterior circulatory territories. These differences are driven by the distinct functional specializations of these brain regions and their corresponding metabolic demands. Nakagawa *et al*[40] investigated the efficiency of dynamic CA in the PCA compared to the middle cerebral artery (MCA) and the effect of cerebral vasodilation due to visual stimulus on these characteristics. The study continuously measured blood flow velocity (BFV) in PCA and MCA and MAP in 45 healthy volunteers with eyes open and an additional 20 subjects with eyes closed and open. Autoregulation was assessed using gains in transfer function across low, high, and cardiac frequency ranges.

The results showed that with eyes open, the gains were significantly higher in the PCA than in the MCA at low (0.03-0.07 Hz) and high (0.07-0.15 Hz) frequencies. Visual stimulation (eyes open) increased BFV and reduced CVR in PCA but not in MCA. This vasodilation was associated with an increase in gain in the low frequency autoregulatory range in the PCA, while the MCA gain remained unchanged. These findings suggest that the previously reported impaired autoregulation in PCA is likely due to visual activation-induced metabolic vasodilation rather than an inherent difference in autoregulation capacity between PCA and MCA[40].

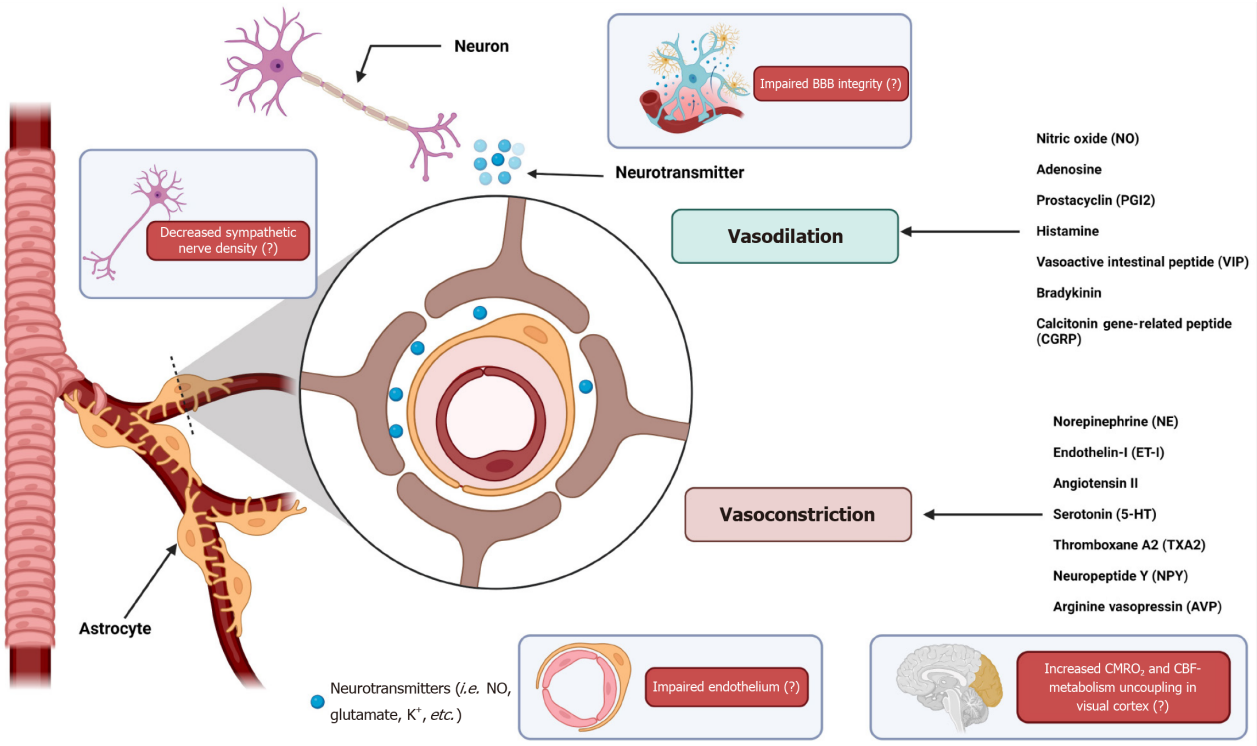

Figure 2 Overview of neurovascular coupling and the blood-brain barrier. Proposed mechanisms of regional variations of cerebral autoregulation include reduced sympathetic nerve density, impaired endothelial function, impaired blood-brain barrier integrity, and CBF-metabolism uncoupling. This figure was generated using BioRender (Agreement No: JM26USH8 LZ).

STUDIES ASSESSING POSTERIOR CIRCULATION CA

Chen *et al*[41] investigated NVC and dynamic CA in PCA among 60 healthy volunteers, identifying no sex differences in these functions. They found that the PCA response to visual stimulation through eyes-open tasks resulted in significantly higher CBF velocity and cerebrovascular conductance index compared to the eyes-closed rest phase. Furthermore, while the gain in PCA during autoregulation was consistently lower than that observed in the MCA at all frequencies, the phase response was similar in both cerebrovascular territories. This study confirms the robust activation of NVC during visual tasks and suggests equivalent functions of dynamic CA and NVC in the PCA between sexes[9].

Chen *et al*[41] explored the impact of cerebral venous sinus thrombosis (CVST) on dynamic CA and NVC in the MCA and PCA during silent reading. The study involved 60 CVST patients and 30 controls, using TCD to measure CBFV and related parameters during visual tasks. The results indicated that the CVST group exhibited impaired dynamic CA in the PCA, particularly in the very low frequency phase, compared to controls. Furthermore, the CVST group showed reduced cerebrovascular conductance and a visual evoked flow response during NVC, suggesting that CVST negatively affects cerebral hemodynamic stability during visual stimulation[41].

Labrecque *et al*[42] investigated dynamic CA and cerebrovascular reactivity to carbon dioxide (CVR_{co2}) in the MCA and PCA in 11 young endurance-trained women. Using a multimodal approach, including sit-to-stand tests and TFA of BP oscillations, the study found no significant differences between MCA and PCA in reduction in CBFV, onset of regulatory response, or rate of regulation during initial orthostatic stress. Although the TFA gain and phase showed location and frequency effects, the normalized gain was similar between the arteries. Absolute CVR_{co2} did not differ significantly between MCA and PCA, but relative CVR_{co2} was 39% lower in MCA. These results suggest that the cerebral pressure-flow relationship is comparable between MCA and PCA in young women, with potential sex-specific differences in CVR_{co2} that require further investigation[42].

PRES

PRES is a clinical and radiological syndrome characterized by headache, encephalopathy, visual impairment, and seizures. It is associated with a range of conditions including severe hypertension, eclampsia, autoimmune diseases, and immunosuppressants. PRES predominantly affects the posterior circulation of the brain, particularly the parieto-occipital regions. The pathophysiology of PRES is closely related to failure of CA, especially in the posterior circulation. Under normal conditions, CA maintains stable CBF despite fluctuations in systemic BP. However, in PRES, this autoregulatory mechanism fails, leading to hyperperfusion and vasogenic edema. Several hypotheses and mechanisms have been proposed to explain this regional vulnerability.

As mentioned above, the posterior cerebral circulation has less sympathetic innervation compared to the anterior circulation, which plays a crucial role in maintaining vascular tone and protecting against rapid increases in BP. The relative paucity of sympathetic nerves in the posterior circulation makes it more susceptible to autoregulatory failure during hypertensive episodes[43]. Additionally, the endothelium of the posterior circulation is more prone to dysfunction due to systemic insults such as hypertension, eclampsia, or cytotoxic drugs. This endothelial injury disrupts the blood-brain barrier and alters autoregulation, leading to vasogenic edema. The vulnerability of the posterior circulation to endothelial dysfunction is also involved in migraine pathophysiology[44]. Furthermore, the posterior regions of the brain have a less robust blood-brain barrier compared to the anterior circulation, making areas such as the parieto-occipital regions more susceptible to breakdown when exposed to high BP or toxic agents, resulting in fluid leakage and edema [45]. The high metabolic demands of the posterior brain regions, such as the occipital lobes involved in visual processing, further strain autoregulatory mechanisms during acute hypertensive crises or toxic insults, leading to a higher propensity to autoregulatory failure and subsequent edema[46].

FUTURE DIRECTIONS ON REGIONAL CA

Future research on regional CA should focus on several key areas to improve our understanding and improve the clinical management of neurological conditions. Large-scale, multicenter studies are needed to validate and expand on the findings related to differential autoregulatory mechanisms in the posterior circulation. These studies should incorporate advanced imaging techniques and dynamic evaluations of cerebrovascular reactivity to provide a more comprehensive understanding of autoregulation under various physiological and pathological conditions. The development and refinement of noninvasive monitoring tools, such as TCD, diffuse correlation spectroscopy, and NIRS are essential for real-time assessment of CA in clinical settings. These tools will enable clinicians to dynamically monitor and adjust therapeutic strategies, improving the management of acute brain injuries and chronic cerebrovascular conditions. The relationship between resting and active cerebral metabolism and O_2 consumption and its effect on CBF and autoregulation is yet to be fully understood. Differences in endothelial function and blood-brain barrier capacity in regional CA are also further areas of research[47]. Additionally, sex-specific differences in CA and cerebrovascular reactivity warrant further investigation.

CONCLUSION

CA is a vital process that ensures stable CBF despite fluctuations in CPP. This mechanism is crucial for maintaining brain function and preventing damage from hyperperfusion or hypoperfusion. Our review underscores the significant differences in the autoregulatory mechanisms between the anterior and posterior circulatory territories of the brain. The susceptibility of the posterior circulation to autoregulatory failure, as seen in conditions like PRES, highlights the need for targeted therapeutic interventions. The unique challenges in managing CA in conditions such as TBI and subarachnoid hemorrhage further emphasize the need for precise, region-specific approaches. Several mechanisms contribute to these regional differences, including variations in sympathetic and parasympathetic innervation, CBF-metabolism coupling, endothelial function, and integrity of the blood-brain barrier. The relative lack of sympathetic innervation of the posterior circulation, combined with its higher metabolic demands and less robust integrity of the blood-brain barrier, may make it particularly vulnerable to autoregulatory dysfunction during systemic insults. Understanding these regional differences in autoregulation can help tailor therapeutic interventions to maintain optimal cerebral perfusion and prevent ischemic or hemorrhagic damage, ultimately improving patient outcomes in critical care settings. Moreover, advancing knowledge of CA can guide the development of novel monitoring techniques and therapeutic strategies that are specific to the affected circulatory territory. Advancing our understanding of regional CA is crucial for improving the diagnosis, prognosis, and management of various cerebrovascular disorders.

FOOTNOTES

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